Appln. No. 09/989,388 Amd. dated October 9, 2003 Reply to Office Action of July 15, 2003

## Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:
Listing of Claims:

Claim 1 (Currently Amended): A Lys-Lys binding site I which is a plasminogen fragment consisting of Kringle 1 to Kringle 3 of a naturally occurring plasminogen with the N-terminal being lysine, which binding site binds to heparin and has the following properties:

- a. a molecular weight of 38 kDa;
- b. it is not glycosylated;
- c. it binds intensely to heparin at pH lower than neutral pH but does not bind to heparin at neutral or higher pH, under non-physiological conditions but binds less intensely to heparin under physiological conditions;
- d. it inhibits tumor metastasis and tumor growth but has no ability to inhibit growth of endothelial cells of blood vessels;

wherein said plasminogen fragment is prepared by;

a. preparing Lys-plasminogen from naturally occurringhuman plasminogen either by adding plasminogen to a

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solution of naturally occurring plasminogen or by incubating naturally occurring plasminogen in the presence of transexamic acid to autolysis;

- b. treating the Lys-plasminogen obtained in step

  (a) with the elastase to produce fractions of the fragment

  comprising Kringle 1 to Kringle 3;
- c. identifying the fragment of Kringle 1 to Kringle 3 which binds to heparin.

Claim 2 (Currently amended): A process for preparing a plasminogen fragment consisting of Kringle 1 to Kringle 3 of a naturally occurringhuman plasminogen with the N-terminal being lysine, said fragment having the ability to inhibit tumor growth, but having no ability to inhibit growth of endothelial cells of blood vessels, comprising;

- a. preparing Lys-plasminogen from naturally occurring plasminogen either by adding plasmin to a solution of naturally occurring plasminogen or by incubating naturally occurring plasminogen in the presence of tranexamic acid to autolysis;
- b. treating the Lys-plasminogen obtained in step
   (a) with elastase to produce fractions of the fragment
   consisting of Kringle 1 to Kringle 3;

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- c. identifying the fragment of Kringle 1 to Kringle 3 which binds to heparin; and
  - d. isolating the fragment which binds to heparin.

Claim 3 (Currently amended): The process according to claim 2 wherein the fragment which bind binds to heparin is recovered by passing a solution of a Lys-plasminogen lysate with elastase through a carrier to which heparin is coupled as a ligand to adsorb those fragment fragments which bind to heparin, and eluting those fragments which do not bind to heparin.

Claim 4 (Currently amended): A composition for inhibiting <u>lung</u> tumor metastasis and <u>lung</u> tumor growth comprising an effective amount of a fragment according to claim 1 and, optionally, a pharmaceutically acceptable carrier.